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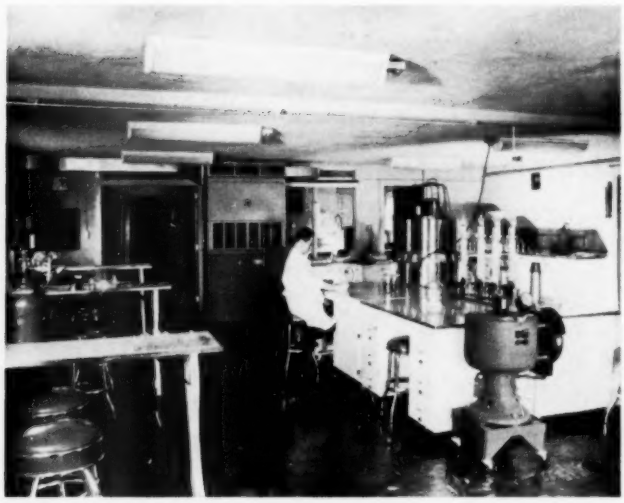

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AMERICAN JOURNAL OF PHARMACY VOL 123 AUGUST 1951 NO 8

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American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

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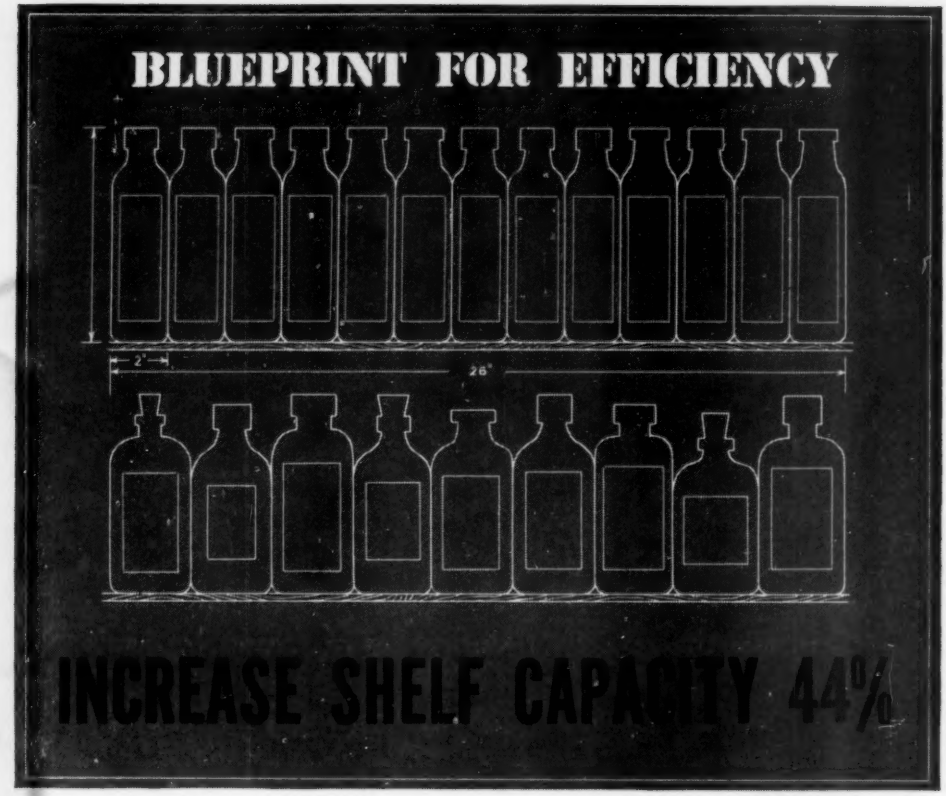

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E D I T O R I A L

THE PHARMACIST AND HIS COMMUNITY

OVER the past several decades the relative positions of the pharmacist and the physician in their relations with the layman have changed considerably. The pharmacist at one time was a man whose austere personage caused his customer to stand in his presence hat in hand and with a feeling almost approaching that of fear. The prescription room was sacrosanct and few indeed had seen beyond its forebiding barriers. What a change, today, when the drug store is often a community center and the pharmacist-proprietor a counselor, friend and guide on all matters pertaining to health supplies as well as life, liberty and the pursuit of happiness. Young people at times confide in him things they would not tell their own parents; and persons who are confused or in distress look to him as a haven of refuge and one on whom the ordinary citizen can depend for almost any kind of information.

The physician, on the other hand, in times past was a person's most intimate associate next to one's spouse. He knew the most personal family secrets, attended all births, weddings, funerals and church suppers. Entrusted to his strict code of ethics were matters which besides himself only the priest might know. No one understood more fully or was loved more genuinely than the family doctor. It is on this heritage that the solid faith of the public in the medical profession now rests. But what has happened in the field of medicine in recent years? The old-time family doctor is a career no longer sought by the young physician. Today is the era of specialization. The medical profession is not alone to blame for this. The laity has come to expect and almost demand the services of a specialist for almost every ill or affliction. The general practitioner is only too often criticized if he fails to refer his patient to a specialist even for the relatively simple diseases. He finds little glamor and satisfaction in simply serving as an agent for referring patients to the experts. Of course, the practice of medicine has become exceedingly complex and no one physician can hope to keep abreast of the many new techniques of diagnosis and therapy in all branches of medical science.

There is, therefore, justification for the growth of specialization. But let us see what has happened to the traditional relationship of physician and patient. The specialist, as a rule, sees many if not most of his patients for the first time when they first visit him. Although a case history may be taken, it is cold and impersonal. The specialist cannot hope to elicit the kind of general information which living for years as a neighbor and friend made possible in the old days. The result is that there exists a widening breach between the medical profession and the public and one which is harmful to both groups. The medical profession is fully aware of this situation and great effort is being made to compensate for and correct this defect. The need for a professional public relations expert by the A. M. A. is ample evidence of this situation in medicine.

Let us now return to the situation in pharmacy where our relations with the public grows increasingly more intimate. This poses a problem for pharmacists since we have increasing responsibilities. Gone are the days when a knowledge of drugs alone suffices. The public expects much more and we must meet the challenge. It is claimed that no profession has more daily public contacts than does pharmacy, and our potential, if not actual, effect on public opinion and action is tremendous. Thus our profession stands in a most strategic and crucial position to do either great good or harm. The public is somewhat disgusted and apathetic with the professional politician; the church in some respects has lost much of its influence on people and this is regrettable; schoolmen all too often are under political pressure, and so it goes. Only the professions still retain full public respect, and pharmacy above all has the widest public contacts.

Pharmaceutical educators with vision fully recognize this challenge and are aware of the steps needed to train pharmacists to meet it. The future pharmacist must be both a specialist in the field of medicinals and yet broadly trained in cultural and social concepts.

Pharmacy can go forward and meet this challenge, or fail miserably because of lack of preparedness. Those educators who decide these great issues and so influence the future have a responsibility of great magnitude and one which must transcend all other considerations.

L. F. Tice

METHODS FOR PROLONGING THE ACTION OF MORPHINE

By Patricia A. Kelly*

IN CASES of intractable pain the use of analgesic drugs is widespread. Of these drugs, morphine is the most commonly employed. Its use is not above criticism and it will be readily acknowledged that it has many properties which detract from its undoubted value as an analgesic. For example, it has a transient duration of action since it lasts only two to three hours after administration by the parenteral route thus necessitating frequent injections and consequently disturbing the patient.

Attempts have been made to prolong the action of morphine, and methods for the prolongation of action of other drugs have been applied to morphine. These methods can be classified as physical and chemical. This paper deals principally with the former.

I. *Physical Methods*

Romansky (1) used a mixture of beeswax and peanut oil to produce delayed action in the administration of penicillin. Later, Buckwalter and Dickison (2) and Floyd (3) used aluminium stearate-peanut oil gels for delaying the release of suspended penicillin and hence prolonging blood levels. Both these methods for prolongation of action were applied to morphine and, in addition, an aqueous suspension of sodium carboxymethylcellulose was prepared and tested.

Formulas used were:—

Base A. Oil and beeswax

White Beeswax	2%
Arachis Oil to	100%

The beeswax was melted in the oil, filtered and sterilized by heating in a hot air oven at 150° C. for one hour.

* Department of Pharmacy and Pharmacology, University of Sydney, Australia.

The morphine sulfate was later suspended in the base using aseptic technique. It dispersed quite readily using a sterile mortar and pestle.

Base B. Oil and Stearate

Aluminium Tristearate	2%
Arachis Oil to	100%

The aluminium tristearate was dispersed through the oil using a tissue homogeniser at full speed for 15 minutes. It was then carefully heated to within the range 117° to 122° C. with constant stirring. The product was then sterilized by heating in a hot air oven at 150° C. for one hour. The morphine sulfate was later suspended in the base in the same manner as for Base A.

Base C. Aqueous Cellulose Base

Sodium Carboxymethylcellulose	1%
Phenylmercuric Nitrate	0.002%
Distilled Water to	100%

The sodium carboxymethylcellulose was heated in a hot air oven at 150° C. for one hour and then sprinkled on to the warm, sterilized phenylmercuric nitrate solution using aseptic precautions. The morphine sulfate was later dissolved in the base aseptically.

Each base was sterilized by an accepted method in order to ascertain whether the temperatures required for sterilization would have any effect on the final preparation. In the case of Base C where it would be logical to sterilize by the official (B. P.) method of "heating with a bactericide" adding the morphine sulfate before finally sealing, it was found that this method caused loss of viscosity of the preparation and since this was considered a vital factor the method given was adopted. The viscosities were, in all cases, such as to enable easy withdrawal into a syringe.

II. *Chemical Methods*

A. A commercial sample of morphine mucate was injected.

B. Morphine Glucoside.

Casparis (4) reported formation of glucosides and their effect on potency. Tetracetyl glucoside was dissolved in water and injected in the same concentration as previously.

Assay Technique

The rat analgesic method of Thorp (5) was used and intramuscular injections of the preparations were given into the thigh muscle of the hind limb. All injections were given at a strength comparable with that which would be used for man, 10 mg/ml, and since the dose in all cases was 5 mg. per Kg. the Trevan micrometer syringe was used to inject the small quantities required.

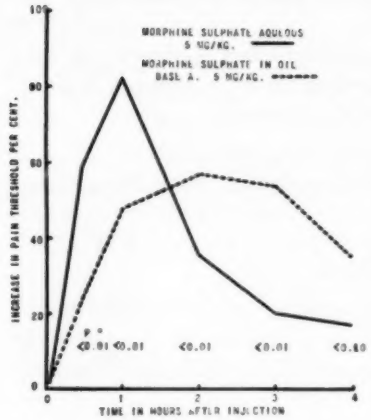
Pain threshold measurements were taken initially and again at intervals of ½, 1, 2, 3, 4 and in some cases 5 hours after injection. A control group of rats was injected with an aqueous solution of morphine sulfate in the same volume and of the same strength on each occasion. Groups of 10 rats were used for each preparation and the mean percentage rise in pain threshold is shown in the relevant graph. This form of assay does not give the maximum possible precision for a given number of animals and it would have been better to have used a "cross-over" design in which the same rats are given each preparation on two different days, half of them receiving the test preparation and half of them the standard on the first day, and the treatments reversed some days later. In the present case, the results obtained tend to be less precise and to show greater variability from animal to animal then the "cross-over" test would have indicated. The method of calculation appropriate in the present case was an analysis of individual responses to the test material and to the standard at each hour followed by the calculation of the significance of the difference between the two preparations using "Student's" "t" test. In the case of morphine mucate the results are so similar to those of morphine sulfate that further calculation would obviously have been redundant. Furthermore, this method of calculation gives a conservative estimate of significance so that, tested by more refined experimental designs, the differences should be even more clear-cut.

Results

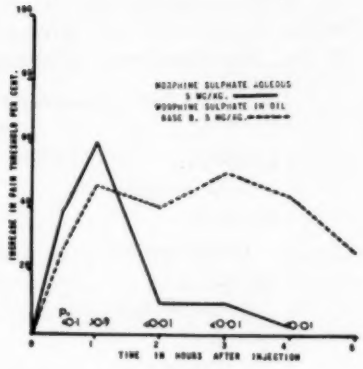
I. *Physical*

Graph A. Shows the prolongation of action of the morphine in the oil-beeswax suspension in comparison with the typical rapid rise and fall curve of the aqueous morphine sulfate.

Graph B. The morphine absorption is here well delayed. This is perhaps the best of all the preparations for the length of time the action is prolonged at a satisfactorily high pain relieving level.


MORPHINE SULPHATE AQUEOUS
5 MG/KG.
MORPHINE SULPHATE IN OIL
BASE A. 5 MG/KG.
INCREASE IN PAIN THRESHOLD PER CENT.
TIME IN HOURS AFTER INJECTION

GRAPH A.

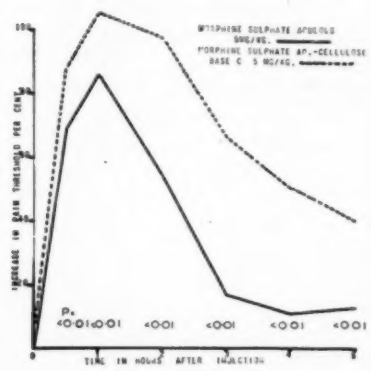

MORPHINE SULPHATE AQUEOUS
5 MG/KG.
MORPHINE SULPHATE IN OIL
BASE B. 5 MG/KG.
INCREASE IN PAIN THRESHOLD PER CENT.
TIME IN HOURS AFTER INJECTION

GRAPH B.

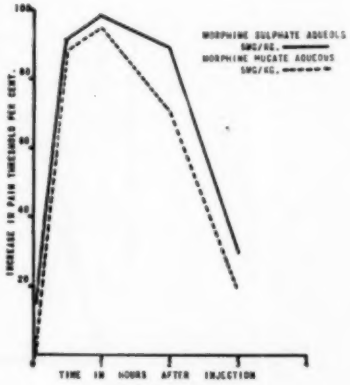
Graph C. This preparation shows a rapid and increased rise over morphine sulfate but the return to normal is also considerably more rapid than that of the aluminium stearate-oil suspension.

II. *Chemical*

Graph D. The results indicate that the commercial sample of morphine mucate tested does not significantly differ from that of morphine sulfate in its duration of action.



GRAPH C.



GRAPH D.

Graph E. No significant analgesic action is exhibited by the Morphine Glucoside.

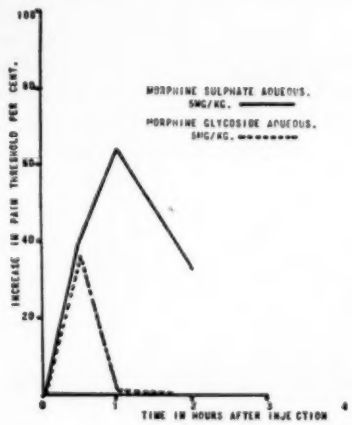
In the following table the ratio of total effect is shown. It will be seen that the best utilization of the drug occurs in the case of Base B. (i.e., the Aluminium Tristearate-Oil preparation).

Table Showing Ratio of Total Effect

	Aq. Morph. Sulph.	Test Preparation
Graph A. (oil-beeswax)	1	1.14
Graph B. (oil-stearate)	1	2.26
Graph C. (aq.-cellulose)	1	1.90
Graph D. (Mucate)	1	0.9
Graph E. (glycoside)	1	0.2

Summary

In an endeavour to prepare a slow-release formula for administration of morphine three physical methods and two chemical were investigated. The physical methods showed superior results to the chemical.



GRAPH E.

It has been shown that an effective slow-release formula has been prepared.

Ratio of Total Effects of Prolonged Acting Preparations

Oil-Beeswax	Graph A	1.14
Oil-Stearate	Graph B	2.26
Aq.-Cellulose	Graph C	1.90
Morphine Mucate	Graph D	0.90
Morphine Sulphate	*Standard*	1.00

Conclusion

Whilst the results of two of these preparations show promise when tested with animals it would be unwise to advocate their use without clinical trials which are at present being arranged.

Acknowledgments

I should like to thank Professor R. H. Thorp, Professor of Pharmacology and Mr. S. E. Wright, Senior Lecturer in Pharmacy for their advice and criticism and Mr. S. Kruger who prepared the sample of morphine glycoside tested.

REFERENCES

(1) Romansky, *Science, 100,* 196 (1944).

(2) Buckwalter and Dickison, *J. Amer. Pharm. Assoc. Sc. Edit., 37,* 472 (1948).

(3) Floyd, *Quart. J. Pharm. Pharmacol., 11,* 747 (1949).

(4) Casparis, *Boll. Chim. farm., 89,* 309-18 (1950).

(5) Thorp, *Brit. J. Pharmacol, 1,* 113 (1946).

THE NEWER THERAPY OF AMEBIASIS

A Review

AMEBIASIS, often called amebic dysentery, is a much more common disease than is generally realized. It is not confined to the tropics nor is it always characterized by an acute dysentery in the patient. It is estimated that the presence of *Endamoeba histolytica* can be demonstrated in from 8 to 15 per cent of the general population of almost any country, with the higher figure often exceeded in tropical areas. It has been stated that the incidence in the United States would suggest 11 million cases in this one country alone and some workers have placed the number at 20 to 25 million. Considered from the standpoint of world population the number of infested persons must be almost unbelievable.

Etiology

Intestinal amebiasis is caused by the protozoan, *Endamoeba histolytica,* which has a two-stage life cycle. The trophozoite, which is the mature ameba, lives in the mucosa and muscle of the large intestine or in the liver parenchyma. The non-motile cyst form is found in the intestinal lumen from whence it is expelled in the feces. Such feces, in turn, are responsible for the spread from one person to another through accidental ingestion in food or drink. Cysts are quite resistant and it is estimated that they remain alive in water for several weeks. Even the usual chlorination of water, or freezing, does not destroy them. Since human feces are the primary source of infection, food handlers with amebiasis are a serious hazard. Raw vegetables which have been prepared by such persons or grown in soil fertilized with human excreta are quite hazardous. The cysts have been isolated from the excreta of houseflies and even roaches and rats may be involved in their transmission.

The so-called "human carrier" of amebiasis is actually one who is not sufficiently ill to be aware of his disease. It is not considered likely that a carrier is ever completely healthy although his symptoms may be relatively mild.

The trophozoite of *Endamoeba histolytica* measures from 13 to 35 microns. It possesses a nucleus which is often surrounded by ingested red cells and the ameba is motile by means of finger-like pseudopodia. The cysts are 4 to 20 microns in diameter, are spherical, and usually contain 4 nuclei.

The invasion of the intestinal wall or the liver by the trophozoites causes lesions as a result of several actions. The ameba secretes a cytolytic agent, the tissues are penetrated by the ameboid movements and bacteria then inflame the tissues as secondary invaders. Ulceration of the bowel eventually takes place and this may be mild or severe.

The liver is often invaded following the passage of the organisms through the intestinal wall into the blood stream. They are carried to the liver via the portal circulation. Here abscesses and extensive necrosis may take place. Even the lungs and brain may become involved in some cases.

Diagnosis

There are no typical symptoms of amebiasis and it is claimed that the disease may simulate every known type of intestinal disorder. The patient may have only abdominal discomfort with either constipation or diarrhea. In some cases periods of diarrhea may follow constipation. Many other symptoms may occasionally be present, such as loss of appetite, general lassitude, nervousness, general debility and tachycardia.

Diagnosis can only be made with certainty on the basis of the study of an adequate number of stool specimens. It is very important that a single negative stool not be taken as definite evidence of the absence of the disease, several samples should be examined.

In patients with diarrhea active amebae as well as cysts may be found in fresh stool samples. If the sample is over 2 hours old the active forms will be disintegrated. The cysts are much more likely to be present since they are much more permanent. Special techniques are necessary in preparing slides for the microscopic identification of either the active trophozoites or the cysts. Only workers trained in these techniques should attempt the examination of feces for these organisms, for a positive diagnosis is based largely on such examinations.

The physician may also wish to sigmoidoscope the patient, not only to detect the presence of amebic ulcers but also to obtain a fresh specimen of feces or mucous for immediate microscopic examination.

Treatment

The treatment of amebiasis is complicated by the fact that drugs which are effective in eradicating the intestinal phase of the disease do

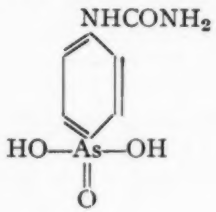
not eliminate the organisms from the liver, and vice versa. Furthermore, it is not possible to rule out liver invasion even in the absence of symptoms which indicate its involvement. For this reason many physicians choose to use combined therapy in all cases.

For many years emetine hydrochloride has been used as a specific to control acute amebiasis and for the liver abscesses of this disease. The dosage schedule recommended by various authorities differs somewhat. One regimen is 60 mg. a day, by subcutaneous injection, for 10 days. Another suggests 60 mg. every 12 hours for 6 doses and in less severe cases 40 mg. every 12 hours for 6 doses.

One of the chief disadvantages of emetine therapy is its toxicity to the heart muscle. Great care must be exercised during its use and some physicians prefer their patients to be hospitalized during its use.

The drug Chloroquine Phosphate (Aralen), which primarily is an antimalarial agent, has shown considerable promise as a means of controlling the liver involvement of amebiasis. Its use is based upon the fact that it localizes in the liver building up a concentration 400 to 600 times that in the plasma. It is given in doses of 0.3 Gm. twice a day for 2 days and then 0.3 Gm. daily for 12 to 19 days. At the same time that emetine or chloroquine therapy is begun the patient should be given some other amebicide to accomplish their eradication from the intestine.

Among the arsenicals, Carbarsone and Phenarsone Sulfoxylate are useful drugs. These are given in a dosage of 0.25 Gm. twice a



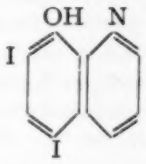
Carbarsone

day for 10 days. Following a 10 day rest period a second course of therapy may be needed. Carbarsone may also be used in retention enemas. For this purpose 2 Gm. of the drug is dissolved in 200 cc. of warm 2 per cent sodium bicarbonate solution and this administered following a cleansing alkaline enema. Such an enema is given every

other night for a maximum of 5 doses. When using Carbarsone in retention enemas oral administration should be suspended.

The arsenicals may cause some toxic effects including dermatitis. fever, vomiting. If these are severe the iodine compounds should be substituted at once.

The iodine compounds Diiodoquin and Iodochlorhydroxyquin are also useful amebicides. Diiodoquin, chemically, is 5, 7-diiodo-8-hydroxyquinoline. It is given at a dosage of ten 0.21 Gm. tablets a day for 20 days. Iodochlorhydroxyquin differs from diiodoquin only

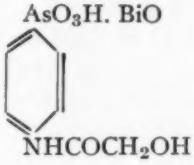


Diiodoquin

in the replacement of one iodine atom with a chlorine at position 5. It is administered orally at a dosage of 0.75-1.0 Gm. daily in divided doses for ten days. After a rest period of a week or ten days a second course of therapy may be needed.

Some physicians prefer combined emetine, arsenic and iodine therapy for intestinal amebiasis. One authority recommends 0.25 Gm. of Carbarsone three times a day until 12 doses have been taken. The arsenical is first taken before breakfast on the day emetine therapy is to be instituted. After the administration of Carbarsone is stopped 0.25-0.5 Gm. of diiodoquin is given three times a day for 7 days. The whole course—emetine, Carbarsone and diiodoquin, is then repeated. With this regimen 22 days are required for a complete treatment.

A relatively new drug for amebiasis is bismuth glycolylarsanilate sold under the proprietary name, Milibis. It has the following structure:



Milibis is insoluble in water and contains 15.01 per cent of arsenic and 41.88 per cent of bismuth. When tested *in vitro* it has a much greater amebicidal action than either Carbarsone or emetine. Clinically, it has proven very effective in amebiasis and it is believed to be superior to both the iodine compounds as well as Carbarsone. It is given in a dosage of 0.5 Gm. three times a day for seven days. A further course of treatment may be needed should positive stools continue.

Certain of the antibiotics have given evidence of being of great value in amebiasis. Some antibiotics probably act only to control the secondary bacterial invaders which so frequently are found associated with the amebae. It is by such a mechanism that penicillin apparently acts since this drug produces improvement in the patient but not a cure. Bacitracin has been found fairly effective and oral tablets for use in amebiasis are available.

Aureomycin and Terramycin appear to be the most effective antibiotics for intestinal amebiasis but at present it seems difficult to say definitely whether one of these drugs is superior to the other. They are given in amebiasis at a dosage level of 2 Gm. per day for 10 days. Following such therapy, the relapse rate is 10 per cent or less after a few weeks following cessation of therapy.

Only time will decide what therapeutic regimen for amebiasis is the best but there can be no doubt that there are far more cases requiring therapy than is generally believed. The excellent drugs which are now available for amebiasis deserve a much more widespread use.

SELECTED ABSTRACTS

Large Doses of Progesterone in Delaying the Onset of Labor. Eichner, E. and Kunin, K. *Am. J. Obst. Gynecol. 61*:653 (1951). Large doses of progesterone were given in an effort to delay the onset of labor and to abort early active labor in 14 consecutive patients with spontaneous premature rupture of the membranes. It was pointed out that even a delay of one week during the critical period of the 24th to 30th week of gestation may spell the difference between a child capable of extrauterine existence and one not capable.

Each of the patients received penicillin daily in an attempt to prevent amnionitis, a known cause of labor. Progesterone was administered intramuscularly in doses up to 200 mg. and repeated twice a day. In some cases the dosage was reduced as low as 100 mg. but never earlier than the fifth day of hospital stay. Upon discharge from the hospital progesterone was continued in doses of 50 to 100 mg. one to three times a week, but not longer than the 34th week of the gestation period.

Four of the patients were in active labor upon admission and up to 400 mg. of progesterone did not prevent delivery. None of these infants lived but convalescence for the mother was uneventful. In the other patients labor was delayed from over 5 days to term. None of the infants lived among the 3 deliveries on the sixth hospital day.

None of the patients in this small series developed sepsis or showed unusual morbidity even though foul lochia was present in four. There were also no recognizable fetal abnormalities. The uncorrected fetal salvage rate was 21.4 per cent. The authors stated that the delay in the onset of labor was greater than that statistically predicted apart from the use of large doses of progesterone.

A Study of the Presence of Intrinsic Factor in Extracts of Hog Stomach and Duodenum. Hall, B. E., Bethell, F. H., Morgan, E. H., Campbell, D. C., Swendseid, M. E., Miller, S., and Cintron-Rivera, A. A. *Proc. Staff Meet. Mayo Clinic 25*:105 (1950). The oral administration of vitamin B_{12} in the treatment of pernicious anemia requires the presence of a potentiating agent, the intrinsic

factor of Castle, for effective utilization. This factor is available in extracts of hog stomach and hog duodenum as well as in the gastric juice of normal human beings.

A series of studies were performed on 13 patients with pernicious anemia in severe or moderately severe relapse. As a result of these studies it was found that the insoluble non-dialyzable fraction of a saline extract of hog duodenal mucosa possesses the activity of an intrinsic factor. However, its activity is considerably less than that of the soluble non-dialyzable fraction. Variable results were obtained from the use of a dilute hydrochloric acid extract of ground whole duodenum of the hog. However, no evidence was found that there is a difference in the amount of intrinsic factor present in extracts made from the proximal 3 feet and the contiguous 4½ feet of duodenum. These studies would seem to indicate that the activity of the intrinsic factor of hog duodenal mucosa is considerably greater than that of the entire duodenum.

A study in one case comparing the effect of heating hog duodenal mucosa, which destroys the intrinsic activity, with incubating the mucosa along with vitamin B_{12} and then heating, showed that greater heat stability was obtained. It was suggested that a complex is formed between the intrinsic factor and the vitamin B_{12} which has greater heat stability than the intrinsic factor alone.

Therapeutic Use of Massive Doses of Ascorbic Acid in Virus Diseases. Klenner, F. R. *South. Med. & Surg. 113*:101 (1951). Massive doses of vitamin C proved to be quite effective in the treatment of various virus infections, according to the report of the author. The most important results were obtained in the treatment of poliomyelitis. Two case histories were given. One, an 8-year-old boy with symptoms of oncoming poliomyelitis recovered completely following the administration of 26 Gm. of ascorbic acid in 48 hours. Thiamine hydrochloride was given over a period of about 3 months thereafter.

The itch of measles or chickenpox and the pain of mumps could be fully controlled within 1 hour and an attack aborted or modified following an intramuscular dose of 250 mg. per Kg. with a dose of half this amount 8 hours later. One of the case histories given was that of an infant with pre-measles symptoms. Sixty-five mg. per Kg.

was given intramuscularly every 4 hours. The temperature dropped and the symptoms disappeared only to reappear when therapy was discontinued and to disappear again when therapy was re-instituted.

A case history was given of an adult with virus pneumonia complicated with encephalitis in which the sulfonamides and antibiotics had failed. Four grams of ascorbic acid were given intravenously followed by 2 to 4 Gm. every 2 to 3 hours. The time interval was later prolonged to every 12 hours but treatment was continued for 2 weeks. The temperature of the patient dropped within 11 hours and cure was eventually achieved. Three other case histories were given in which cures were obtained from the use of the vitamin in pulmonary virus infections.

The author reported, also, that a synergistic effect had been observed in a small series of pulmonary virus infections between calcium gluconate or calcium levulinate and ascorbic acid. Glycosuria was found in all of the patients with virus infections upon admission. This cleared completely with ascorbic acid therapy. Some toxic effects, such as diarrhea, endothelial irritation, fainting, and rash, were observed in some of the patients.

Treatment of Protozoan Diseases With Antibiotics. Shookhoff, H. B., *Bull. N. Y. Acad. Med. 27*:439 (1951). The author reported results obtained in the treatment of protozoan infections with bacitracin, aureomycin and terramycin. Bacitracin was given in doses of 60,000 units per day for 5 days in 22 patients and for 10 days in 3 patients with *Endamoeba histolytica* infection. Eighteen of the patients were cured and were followed for an average of 5 months. Mild side effects, such as digestive disturbances and transitory skin eruptions, were observed in 13 of the patients.

Aureomycin in doses of about 1 Gm. per day benefited 22 of 24 patients treated. During the follow up period, which averaged 4½ months, an average of 4½ stool examinations were performed. The toxic effects which appeared were more distressing than those observed with bacitracin. Nausea, diarrhea, and anal irritation varying from slight itching to a severe peri-anal inflammation occurred in a high percentage of the patients.

Terramycin was given to 6 patients in a total amount of 4 to 8 Gm. in 4 to 5 days. Two of the 6 who had received 4 Gm. still showed *E. histolytica* in the stools after treatment. Re-treatment with

6 Gm. in 4 days produced negative stools in 1 of these patients. Toxic effects were observed including anal irritation, abdominal cramps and diarrhea. The diarrhea was severe in 1 patient.

Three of 5 patients with amebic hepatitis were improved with aureomycin and one patient with hepatitis treated with bacitracin showed clearing of the stools but no symptomatic improvement. Each case of hepatitis was cleared with chloroquine.

Penicillin in Pulp Capping. Gilberg, S. L. *U. S. A. F. Med. J. 2*:203 (1951). Pulp capping has always been considered a hazardous procedure. There is a persistent belief among dentists that once the pulp is exposed it is doomed and if it is exposed as a result of caries it is doomed beyond a question of a doubt.

Bacteriologic studies of caries-affected areas of teeth have shown various organisms, including *Streptococcus pyogenes, Streptococcus brevis, Streptococcus viridans, Staphylococcus aureus, Staphylococcus albus,* gram-positive diplococci, and gram-positive and negative bacilli. Penicillin is highly effective against the organisms commonly invading the dental pulp.

The author treated 205 teeth with pulp cappings where the caries had invaded the pulp. Complete debridement of the caries was performed under local anesthesia. The tooth was then isolated, the cavity was washed with warm water and dried. A 50,000 unit tablet of penicillin was divided into two portions. A drop of sterile distilled water or lime water was placed over the exposure and the half-tablet of penicillin placed in it. A thick paste of zinc oxide, the remainder of the penicillin tablet and distilled water or lime water was prepared and the exposure was carefully covered. Then a heavy mixture of zinc oxide, eugenol and silver nitrate crystals was made and the cavity shaped to the correct contour for the type of filling it was to receive. This forms a hard base which eliminates repeated grinding operations on the tooth and avoids the possibility of disturbing the capping. An amalgam filling should then be applied within 2 weeks.

The capping was considered a failure if severe odontalgia or neuralgia persisted for more than 24 hours after the capping procedure. There were but 5 failures among the 205 cappings performed in this manner.

The authors present this evidence in support of the successful potentialities of pulp capping with penicillin.

The Local Use of Coal Tar and Antihistamine Combination. A. J. P. Walters, J. D., and Gilman, R. L. *U. S. A. F. Med. J, 2*:187 (1951). An ointment containing 5 per cent coal tar and 2 per cent pyranisamine maleate in a hydrophilic base was applied topically for the treatment of a variety of dermatoses and pruritis in a total of 52 persons. Previous treatment had extended over a period of 1 to 10 years and varied extensively.

The authors reported that 71 per cent of the patients showed good results with respect to their dermatosis and 75 per cent showed good results in the relief of their pruritis. Good results meant that there was definite improvement in the dermatosis and the pruritis. The conditions diagnosed as psoriasis and senile pruritis showed the least favorable response in that good results were obtained in about 50 per cent of the cases.

An examination of patients who could not tolerate the ointment or who experienced poor results, revealed no evidence of the development of sensitivity. However, the authors suggested that such a reaction could be expected occasionally in a larger series of patients. No incompatibilities were observed when this combination was used in conditions which could normally be expected to yield favorable results with preparations containing coal tar alone.

The combination of coal tar and pyranisamine maleate appeared to have a synergistic action for, about a 20 per cent increase in effectiveness was observed in this series as compared with the normally anticipated effectiveness of coal tar alone. However, the authors stated that no curative value as such was apparent other than that which might be expected to follow from a more prompt relief of the pruritic condition.

Effect of Histamine Desensitization on Histamine Induced Gastric Secretion of Guinea Pigs. Ambrus, J. L. Ambrus, C. M. and Harrisson, J. W. E., Gastroenterology (Baltimore) *18*, No. 249-253, June (1951). Antihistamines, although inhibiting most effects of histamine, do not influence histamine induced gastric secretion. Administration of graduated doses of histamine decreases the sensitivity of guinea pigs toward this substance, the sensitivity being established by the aerosol method, previously described by the authors (Harrisson, J. W. E., Ambrus, J. L., and Ambrus, C. M.: *J. A. Ph. A.* Scientific Ed. *40*, 226 (1951). Guinea pigs rendered thus resistant toward histamine also show diminished gastric secretory response to

histamine. If during desensitization treatment each injection of histamine is preceded by an injection of antihistamine, the same degree of resistance develops toward histamine. Daily administration of histamine to guinea pigs usually results in the production of gastric ulcers; no ulcer formation was observed in the histamine desensitized group. The mechanism of this phenomenon is briefly discussed.

The Use of a Cation Exchange Resin in Hypertension. Groff, D. N. *N. Y. State J. Med. 51*:758 (1951). The author first reviews the evidence which has accumulated for the depressive effect on the blood pressure of persons with hypertension when treatment includes a low salt diet. Evidence is also presented which fairly well narrows the cause of this depressive effect to the removal of the sodium ion rather than of the chloride ion. Thus, the author concluded that it was reasonable to anticipate that the administration of a cation exchange resin of the carboxylic type, which would remove sodium and other cations from the alimentary tract, would produce a depression in blood pressure in hypertensive patients.

A small preliminary group of six ambulatory patients with hypertension of varying degrees were maintained on a low salt diet and treated with the exchange resin. In all cases a significant lowering of the blood pressure was obtained. The patients also experienced an increased feeling of well-being and an increased ability to work. They also noted a relief of anginal seizures and exertional dyspnea. The improvement in two patients was such that they stopped coming for treatment and so did not continue the full six-month period.

The dosage employed most satisfactorily was one tablespoonful of resin before each of the three daily meals. One patient experienced some nausea from the resin but no serious side effects were observed. Experimentally the resin had previously been shown to be non-toxic when incorporated to a level of 5 to 10 per cent in the normal diet of the rat.

Acute Leukemia Treated With A-Methopterin. Dacie, J. V., Dresner, E., Mollin, D. L., and White, J. C. *Brit. Med. J.* No. 4710:784 (1951). The effect of the folic acid antagonist a-methopterin was studied in seven cases of acute leukemia, five of the cases being children. In only one case was there evidence of a beneficial

effect, a case of lymphoblastic leukemia in a child, and this was of short duration.

The child showing a temporary improvement received 22.5 mg. of a-methopterin in nine days. There were severe toxic manifestations resulting from the drug as manifested in a deterioration of general condition, development of leucopenia, bleeding from the gums with petechial mucosal hemorrhages and hematuria, and repeated vomiting. However, the joint symptoms subsided and visceral enlargement regressed, there was an improvement in the state of the peripheral blood and bone marrow, and, subsequently, there was an improvement in the general condition of the child. This clinical remission lasted for less than four weeks in spite of maintenance doses of a-methopterin of 2.5 mg. twice a week. Degeneration occurred quickly and death followed within a few days.

Severe bleeding complicated treatment in every case and when it was present before the administration of a-methopterin the drug increased this complication. This hemorrhagic condition is not controllable by intravenous protamine sulfate or by toluidine blue. A number of authors have reported that in those cases in which a-methopterin or aminopterin is successful in inducing an initial remission in human acute leukemia, resistance to further therapy rapidly develops during subsequent relapses. This acquired resistance appears to be similar to the development of drug resistance by bacterial cells.

Antabuse Therapy of Alcoholics. Brown, C. T. and Knoblock, E. C. *U. S. A. F. Med. J. 2:*191 (1951). In man the administration of Antabuse (tetraethylthiuram disulfide) is relatively nontoxic but when a person conditioned with Antabuse ingests a small amount of alcohol a series of intensely unpleasant symptoms is inaugurated within a few minutes. How far the patient goes into the series of symptoms known as the "acetaldehyde syndrome" is largely a function of the alcohol intake. In some cases the acetaldehyde syndrome assumes alarming proportions with a drop in blood pressure to the vanishing point. Oxygen must be administered at this point and can be used to ameliorate the symptoms in any case.

The authors studied the effects of Antabuse on 50 patients who seemed to be sincere in their desire to recover from their illness. The patients were given 2 Gm. of Antabuse on the first day and reduced by 0.5 Gm. until the fourth day. Four days of treatment

are required prior to the first drinking trial in order to develop the primary tolerance. The patients were given one drinking trial on the fifth day and another on the eighth day. Maintenance doses of Antabuse of 0.5 Gm. were given between the trials and afterward. After the second drinking trial the patients were placed on outpatient status and given a one-week supply of the drug. At the end of eight months the authors reported that 40 per cent of the patients were socially recovered, 25 per cent were much improved, 2 per cent were failures,and 33 per cent were not within contact. Those with whom contact was lost were usually lost because they recovered sufficiently to move to another locale and assume a better paying job.

The authors pointed out that Antabuse is not a cure for alcoholism but is to be regarded as merely an adjunct in therapy by which the patient is given a psychologic as well as a physiologic aversion to the poison which is threatening his existence. The low maintenance dose effective in this series is assumed to be due to the high altitude and the consequentially reduced oxygen content of the air.

Blood studies revealed that the acetaldehyde levels of the fasting patients in this study ranged from 63 to 383 micrograms per 100 cc. During the first drinking trial they rose to 305 to 2,844 micrograms per 100 cc. It was also found that the increase in the acetaldehyde levels closely paralleled the increase in that of the blood alcohol. Thus the "acetaldehyde syndrome" was verified.

The authors concluded that Antabuse must be used only on a prescription basis with careful supervision because of the intense reaction which follows the ingestion of alcohol. The use of the treatment was felt to be contraindicated in patients with cardiovascular disease, epilepsy, advanced cirrhosis of the liver, diabetes mellitus, and thyroid dysfunction. The authors also offered their further impressions gained as a result of this study, that (1) the Antabuse-prepared patient cannot drink, (2) although a certain amount of conditioning is inevitable, the prime therapeutic effect is the realization by the patient that he is physiologically intolerant to alcohol, (3) the treatment offers an opportunity for an entirely new psychiatric study of the alcoholic, and (4) the minimum routine clearance in addition to careful history and physical examination, should include cardiac evaluation by means of EKG, urinalysis and the bromsulfalein retention test.

Androgen-Estrogen Treatment in the Menopause. Glass, S. J. and Shapiro, M. R. *GP 3:39* (1951). A critical study of 92 patients produced evidence that a mixture of estrogen and testosterone was more effective in treating the menopausal symptoms than either of the hormones separately. The authors provided a list of 9 advantages for the superiority of this combined therapy.

In the study presented four identical-appearing tablets were used. The first tablet contained 0.25 mg. diethylstilbestrol, the second contained 5 mg. methyl testosterone and 0.25 mg. diethylstilbestrol, the third contained 5 mg. methyl testosterone, and the fourth was a placebo. These four tablets were given to the patients in various orders so that the clinical responses could be properly graded. Final results on each patient were verified by repeated trials. The placebo tablet was the only one known to the clinical investigators and it was used freely to prevent any lag effects between the trials of the various tablets.

The range of dosage for "saturation" during the first 14 to 21 days of treatment was 5 to 10 mg. methyl testosterone, and 0.5 to 1.0 mg. estrogen. For maintenance therapy the daily dosage was 2.5 to 5.0 mg. methyl testosterone and 0.25 to 0.5 mg. estrogen.

Subjective criteria was largely used to determine the effectiveness of the tablets, namely, relief from flushes, sweats, nervousness, palpitation, and arthralgias. The only objective data sought were changes in vaginal cytology, the skin insofar as acne and hypertrichosis were concerned, hypertension, and body weight. The results indicated that 72.8 per cent preferred the combined therapy, 10.9 per cent the androgen, 6.5 per cent the estrogen, and 9.8 per cent did equally well on all tablets (psychoneurotic group).

The authors reported that they had come to the conclusion that the subjective findings served as a more sensitive index than the changes in vaginal cytology. They also did not have to submit any of their patients on the combined therapy to diagnostic curetage for induced withdrawal bleeding. The comfort to the patient, the inherent simplicity, and the clinical responses to combined therapy were so gratifying that the authors now recommend such treatment in the management of the menopausal syndrome.

Intramuscular Injection of Quinidine Sulfate in Propylene Glycol. Gluck, J. L., Gold, H., Greiner, T., Modell, W., Kwit, N. T., Thickman, S., Otto, H. L., and Warshaw, L. J. *J. A. M. A. 145*:637 (1951). The administration of quinidine sulfate for disorders of cardiac rhythm has met with difficulties. Oral administration causes gastrointestinal irritation with pain, nausea and vomiting, and diarrhea in a large proportion of patients. Intramuscular injection of an aqueous solution of the dihydrochloride causes painful inflammatory induration at the site of injection. Therefore, the authors studied the use of a 20 per cent solution of quinidine sulfate in propylene glycol. Tests have shown that propylene glycol does not produce systemic toxicity and the slight tissue inflammation which occurs at the sight of injection does not cause pain or other signs of local reaction. The authors also studied the effect of propylene glycol on the heart and found that it did not affect the electrocardiograms.

The authors gave intramuscular injections of the propylene glycol solution of quinidine sulfate to 19 patients. Twelve patients received only one dose of from 0.2 to 0.6 Gm. for the purpose of studying local reactions. In the seven remaining patients multiple injections were given and the curve action of the heart was also studied. A total of 69 injections were given.

The study revealed that in those patients in which pain or other local reactions occurred at the site of injection they were slight and of short duration. In 2 of 3 patients who received 12 or more injections at intervals of 3 to 6 hours there was some swelling of the soft tissues but there was no pain, induration or slough. The curve of action on the auricle in auricular fibrillation and flutter was shown to be essentially the same as that obtained by oral administration. The peak effect was reached in about 3 hours. About half of the effect wore off in about 8 hours and the effect had disappeared completely in 24 hours.

BOOK REVIEWS

Ion Exchange Resins. By Robert Kunin and Robert J. Myers, Rohm and Haas Company. xi + 212 pages, incl. index. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y., 1950. Price $4.75.

In this book, ion exchange resins are discussed thoroughly, beginning with an explanation of the mechanism of the process, characteristics of various types of resins, methods of synthesis and going on to a consideration of their manifold applications. The latter include water softening and deionization, applications to analytical chemistry, to medicine, biology, and agriculture. Then a chapter is devoted to methods of study of ion exchange resins, and the final chapter deals with the design of exchange units.

A tremendous increase in the laboratory and industrial uses of ion exchange resins has taken place in the last few years. As a result a great deal of new information is constantly being made available, and, because of the widely divergent fields in which these applications occur, this information is widely scattered through the scientific literature. There has been a need for a single, authoritative source for such data, and in this book the authors have succeeded in providing it.

LOUIS A. REDER

Organic Syntheses. Volume 30. Arthur C. Cope, Editor-in-Chief. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y., 1950. vi + 115 pp. 15.5 x 23.5 cm. $2.50.

This volume contains detailed directions for the preparation of 39 organic compounds. As is usual in this series, the directions have been checked in independent laboratories. The syntheses of the following are described: 9-acetylanthracene; 3-aminopyridine; p-aminotetraphenylmethane; DL-aspartic acid; benzoylcholine iodide and chloride; n-butylacetylene; β-carbethoxy-γ, γ-diphenylvinylacetic acid; chloroacetonitrile; trans-2-chlorocyclopentanol; 4,4′-dichlorodi-

butyl ether; diethyl cis-Δ^4-tetrahydrophthalate and diethyl cis-hexahydrophthalate; 1,4-diiodobutane; ethanedithiol; ethylenimine; 5-ethyl-2-methylpyridine; ethyl phenylcyanoacetate; fumaronitrile; glutaric acid; hexahydro-1,3,5-tripropionyl-s-triazine; 2-iodothiophene; 2-mercaptobenzimidazole; methanesulfonyl chloride; N-methyl-2,3-dimethoxybenzylamine; 1-methyl-3-ethyloxindole; methyl β-thiodipropionate; 1-naphthaldehyde; o-nitroacetophenone; phenylacetylene; trans-1-phenyl-1,3-butadiene; α-phenyl-α-carbethoxyglutaronitrile; α-phenylglutaric anhydride; phenylsuccinic acid; 2,3-pyrazinedicarboxylic acid; 1,2,3,4-tetrahydrocarbazole; cis-Δ^4-tetraphthalic anhydride; tetraphenylarsonium chloride hydrochloride; o-tolualdehyde; vanillic acid; vinyl laurate and other vinyl esters. The subject index is for volume 30 only; previous preparations are listed in Collective Volumes I and II and Volume 29.

This volume is the start of the future Collective Volume IV. We may look forward to Collective Volume III in the near future.

N. RUBIN

The Interests of Pharmacists. By Milton Schwebel. 1951. 84 pages, paper-bound. $1.75. King's Crown Press (a division of Columbia University Press), 2960 Broadway, New York 27, N. Y.

There was a time, within the memories of most of us, that admission to a pharmacy school was "had for the asking". Today, however, it is not so simple as that. Questions of motivation, professional heritage, scholastic average and relative standing in the high school, entrance examination results and many other hurdles face the current applicant for admission to the college of pharmacy.

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In this book there is shown the development and the results of an evaluating scale for pharmacists, and applicants for entrance

into the study of pharmacy. The results obtained in a number of samplings in which the author received excellent cooperation from persons in all phases of pharmaceutical endeavors, are quite interesting, if not especially startling.

The entire work, which condenses the results of a tremendous amount of research into 84 pages, should prove helpful to college admissions officers, high school vocational guidance directors, personnel psychologists, industrial relations specialists, and to any one else in any of the various facets of pharmacy.

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